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Quarterly Morbidity & Activity Report

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Meningococcemia without Meningitis: A case study in Bhutan

IN THIS ISSUE:

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Abstract

Acute renal failure is a common occurrence in sepsis but it is not often reported in fulminant meningococcal sepsis (FMS) or meningococcemia. A case study of 16 years old boy who died within 12 hours after referral from BHU (Thinlaygang) to national referral hospital (JDWNRH) revealed that the patient had died from fulminant meningococcal sepsis (FMS) or fulminant meningococcemia with acute renal failure. The patient had high fever, hypotension, thrombocytopenia, purpura fulminans and absence of meningitis during admission but proper diagnosis could not be established.

1. Introduction

Meningococcemia is a serious illness caused by bacterium *Neisseria meningitidis*, with a high mortality rate of up to 40-60%. More than half of patient suffering from meningococcemia dies from shock within 12 hours of hospital admission. Moreover, 11-19% of survivor lives with permanent skin and limb necrosis. Therefore, early diagnosis and administration of adequate antibiotics are essential. In this case report, author presents a death case study of fulminant meningococcemia with acute renal failure which is an important complication of meningococcemia.

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Editorial

QMAR is a special effort made by the Research and Epidemiology Unit and Health Information Unit to update our health colleagues and other partners in health on quarterly health information of the country.
Data gathering is a collective effort of all the health workers at all levels and meaningful usage at all level must to be ensured as we invest a lot of time and money in this process of gathering and reporting data.
Although, because of many challenges we face in collection of accurate and comparable data, the data presented here are very useful in tracking trends of diseases and intervention monitoring.
As mentioned in this report, 30% of the health facilities did not send reports on time and this needs to be corrected since the aim of the QMAR will be defected if we cannot have the country wide data.
All districts whose names are mentioned in this QMAR for not reporting on time are reminded to take actions to send data on time.

(Dr. Lungten Z. Wangchuk)
MBBS, MPH (Epidemiology & Public health Research)
- For the Editorial Team

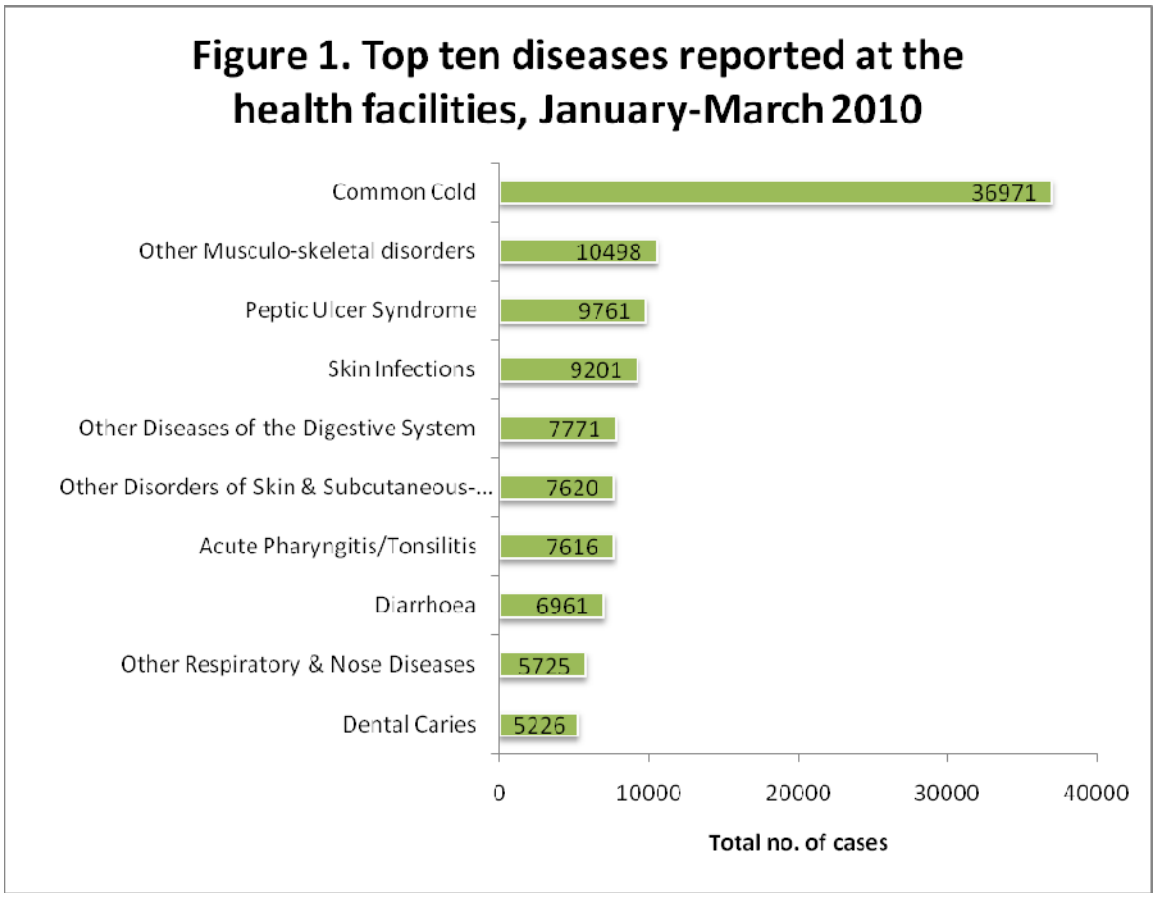
1. Timeliness of the report

The following descriptive analysis includes only 14 Dzongkhags. As per the policy directives of Health Ministry, all Dzongkhags should have sent the 1st quarter data by 15th May 2010. However, the following Dzongkhags have not sent the data on time:

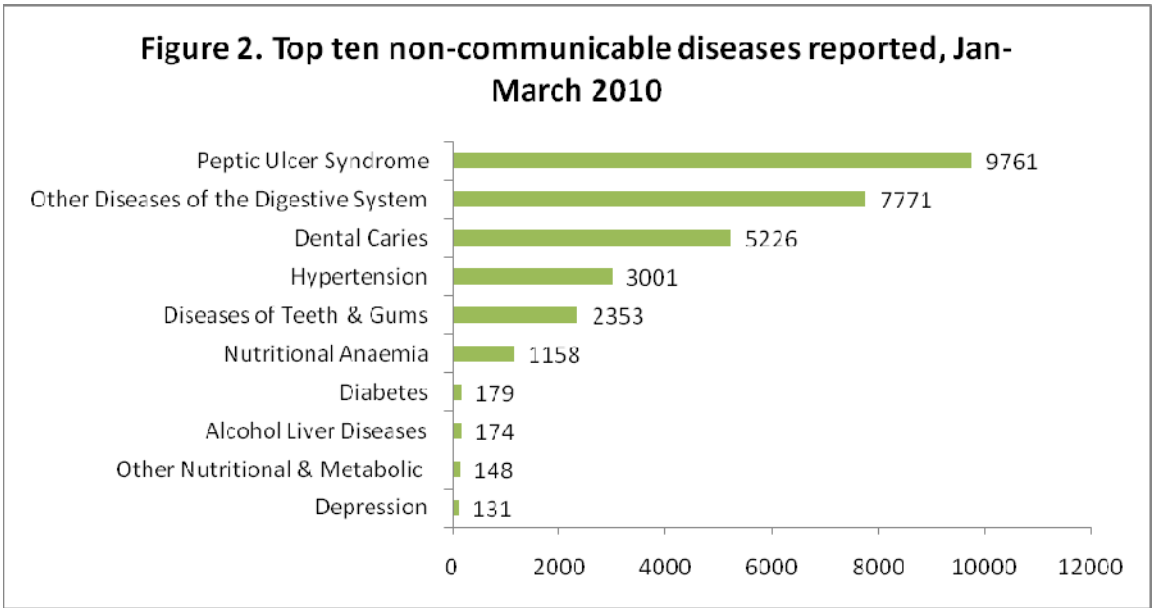
a) Haa
b) Wangdue
c) Trashigang
d) Sarpang
e) Trongsa
f) Thimphu

This report will cover only the data received by Health Management and Information (HMIS) Unit, namely, the morbidity and activity reports. There are many vertical reporting systems and the number varies from district to district. The data of such reporting systems are not included as its reliability and consistency is not assessed.

2. Top Ten diseases reported



3. Top Ten Non-Communicable Diseases reported



4. Ante-Natal Care, Post-Natal Care and Attended Delivery Report

Table 1: ANC and PNC availed at the health facilities, Jan-March 2010

District Name	1st Visit	2nd Visit	3rd Visit	4th Visit	More than 4 visit	PNC 1st Visit	PNC +2 Visit
Bumthang	105	74	59	22	53	25	12
Chukha	306	311	333	340	529	128	73
Dagana	91	86	75	52	35	52	34
Gasa	12	7	9	7	4	5	6
Lhuentse	79	65	55	27	38	52	8
Mongar	223	180	118	121	119	110	75
Paro	201	189	176	119	349	108	12
Pemagatshel	89	95	88	60	71	59	31
Punakha	139	150	124	91	114	103	73
SamdrupJongkhar	189	143	105	72	62	47	13
Samtse	290	251	223	295	237	189	87
TrashiYangtse	87	81	69	62	57	47	41
Tsirang	90	60	50	34	29	41	18
Zhemgang	86	67	56	24	25	31	3
Total	**1987**	**1759**	**1540**	**1326**	**1722**	**997**	**486**

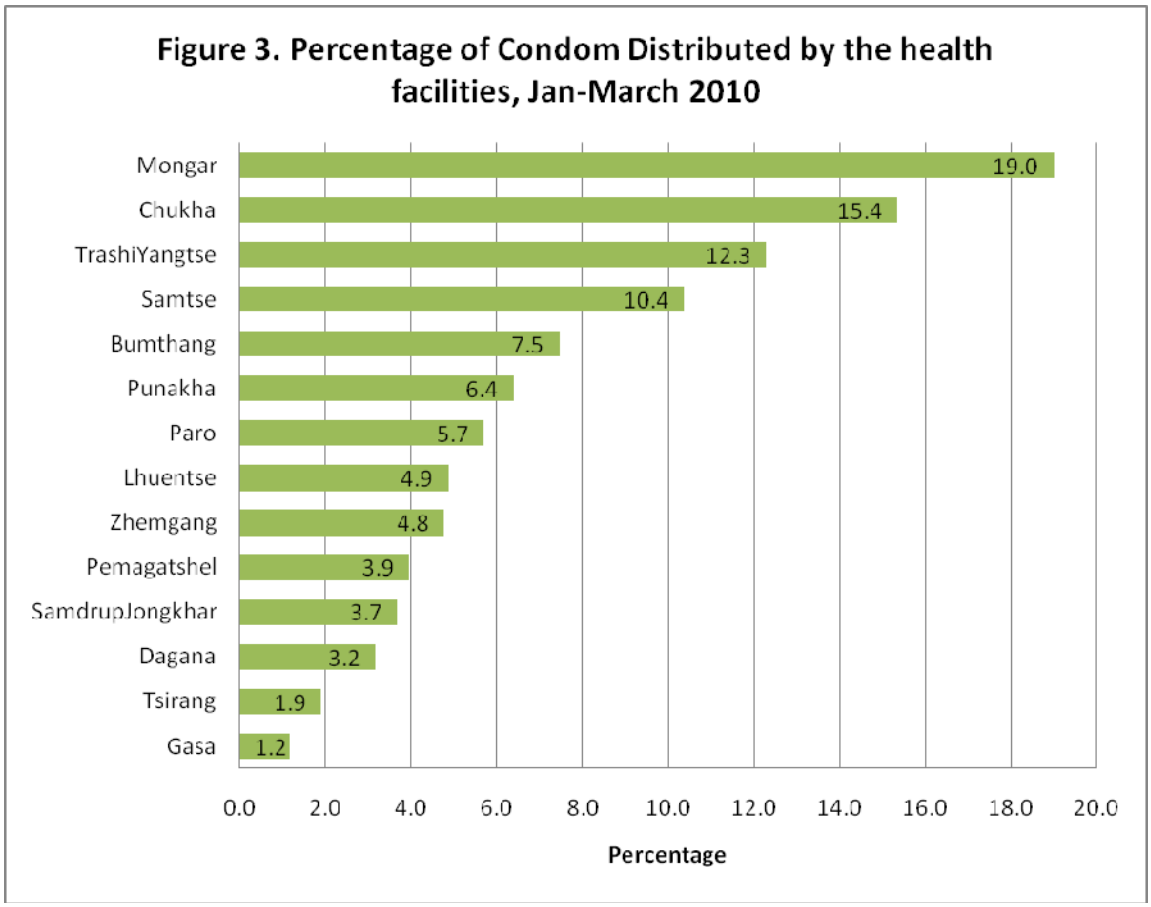
Table 2: TT dose given and attended delivery by the health personnel, Jan-March 2010

District Name	TT 2+	TT Others	Attended Delivery		
			Home Delivery	Facility Delivery	Vacuum Delivery
Bumthang	82	248	7	28	0
Chukha	336	569	11	194	11
Dagana	77	224	2	34	0
Gasa	14	18	1	0	0
Lhuentse	62	162	6	18	0
Mongar	176	289	35	155	2
Paro	167	458	1	88	1
Pemagatshel	65	152	11	39	0
Punakha	78	87	11	81	1
SamdrupJongkhar	154	305	11	75	1
Samtse	272	834	4	134	1
TrashiYangtse	63	108	2	35	0
Tsirang	234	96	1	25	0
Zhemgang	71	114	18	10	0
Total	**1851**	**3664**	**121**	**916**	**17**

5. Family Planning Method Report

Table 3: Different family planning methods availed from the health facilities, Jan-March 2010

District	IUD	Oral Pill cycle	DMPA
Bumthang	2	841	611
Chukha	42	1374	2215
Dagana	3	818	1090
Gasa	15	15	76
Lhuentse	11	255	565
Mongar	31	503	1682
Paro	8	399	832
Pemagatshel	7	318	673
Punakha	21	609	727
SamdrupJongkhar	15	706	1150
Samtse	74	1690	1660
TrashiYangtse	4	136	361
Tsirang	0	552	831
Zhemgang	2	546	740
Total	**235**	**8762**	**13213**



From the total numbers of condom distributed (202122), highest was distributed by Mongar district with 19% followed by Chukha with 15.4%, lowest was Gasa.

6. Admissions

Table 4: Average patient days of different health facilities, Jan-March 2010

District	Total Admission	Absconded	Patient days	Average Patient days
TrashiYangtse	133	0	1321	9.9
Mongar	927	1	6497	7.0
Pemagatshel	83	0	452	5.4
SamdrupJongkhar	461	2	2413	5.2
Punakha	446	2	2075	4.7
Lhuentse	232	5	1031	4.4
Samtse	742	2	3112	4.2
Zhemgang	245	2	992	4.0
Bumthang	132	2	479	3.6
Paro	655	3	1878	2.9
Dagana	35	1	69	2.0
Chukha	1141	3	1930	1.7
Gasa	0	0	0	0.0
Tsirang	0	0	0	0.0
Total	**5232**	**23**	**22249**	**4.3**

7. Laboratory Examinations

Table 5: Laboratory examinations conducted at health facilities, Jan-March 2010

District	Total	Haemoglobin	Blood grouping	Malaria Slides	TB Sputum	Urine	Stool	HIV
Bumthang	1460	508	224	7	24	600	14	124
Chukha	11617	2560	936	725	225	2221	42	383
Dagana	2854	573	183	419	56	842	5	119
Gasa	138	33	37	0	0	51	0	17
Lhuentse	3070	409	123	0	56	594	13	250
Mongar	6800	2241	560	77	435	1892	203	1403
Paro	5264	676	395	17	181	1540	29	191
Pemagatshel	2487	452	247	68	27	696	9	84
Punakha	1905	847	325	17	47	626	23	201
SamdrupJongkhar	4467	1072	348	760	273	1611	27	206
Samtse	7599	2043	784	1105	144	1592	27	301
TrashiYangtse	968	379	142	2	18	338	4	78
Tsirang	11523	475	231	114	5	258	2	73
Zhemgang	4197	451	117	182	30	464	29	47

8. Nutritional status of Children under Five years of age reported

Table 6: Nutritional status of Children under Five years of age reported at health facilities, Jan-March 2010

District	Over weight	Normal weight	Malnourished	Severely Malnourished
Bumthang	212	1404	50	4
Chukha	223	4357	171	5
Dagana	87	1666	173	9
Gasa	8	142	23	0
Lhuentse	88	1214	81	11
Mongar	293	3768	326	31
Paro	130	2553	106	17
Pemagatshel	163	2034	293	11
Punakha	33	1487	34	4
SamdrupJongkhar	123	2245	179	20
Samtse	94	3819	287	21
TrashiYangtse	46	1202	229	5
Tsirang	63	1436	120	12
Zhemgang	121	1269	173	9
Total	**1684**	**28596**	**2245**	**159**

9. Surgical Procedures

Table 7: Surgical procedures conducted at different health facilities, Jan-March 2010

		General						Orthopaedic					
		Abodominal			Others			Estremities			Other		
District	Ceasarian	Major	Minor	Lap*	Major	Minor	Lap*	Major	Minor	Lap*	Major	Minor	Lap*
Bumthang	0	0	0	0	0	0	0	0	0	0	0	0	0
Chukha	50	13	57	0	0	24	0	0	21	0	2	5	0
Dagana	0	0	0	0	0	0	0	0	0	0	0	0	0
Gasa	0	0	0	0	0	0	0	0	0	0	0	0	0
Lhuentse	0	0	0	0	0	3	0	0	0	0	0	3	0
Mongar	32	28	21	2	24	22	0	46	39	0	1	5	0
Paro	29	11	20	0	5	18	0	0	0	0	2	29	0
Pemagatshel	0	0	0	0	0	2	0	0	0	0	0	0	0
Punakha	1	1	1	0	0	28	0	0	0	0	0	0	0
S.Jongkhar	11	8	0	0	0	492	0	8	27	0	0	0	0
Samtse	8	5	19	0	3	92	0	0	1	0	0	134	0
TrashiYangtse	0	0	0	0	0	0	0	0	0	0	0	0	0
Tsirang	0	0	0	0	0	0	0	0	0	0	0	0	0
Zhemgang	0	0	0	0	0	2	0	1	2	0	0	0	0
Total	**131**	**66**	**118**	**2**	**32**	**683**	**0**	**55**	**90**	**0**	**5**	**176**	**0**

	Gynaecology			ENT			EYE		
District	Major	Minor	Lap*	Major	Minor	Lap*	Major	Minor	Laparoscopic
Bumthang	0	0	0	0	0	0	0	0	0
Chukha	1	12	0	0	1	2	0	0	0
Dagana	0	0	0	0	0	0	0	0	0
Gasa	0	0	0	0	0	0	0	0	0
Lhuentse	0	0	0	0	0	0	13	0	0
Mongar	32	34	2	2	12	0	15	3	0
Paro	6	28	0	0	0	0	0	0	0
Pemagatshel	0	0	0	0	0	0	0	0	0
Punakha	0	0	0	0	0	34	0	0	0
S.Jongkhar	2	16	0	0	0	0	0	0	0
Samtse	0	2	0	0	0	0	0	42	0
TrashiYangtse	0	0	0	0	0	0	32	13	0
Tsirang	0	0	0	0	0	0	0	0	0
Zhemgang	0	0	0	2	0	0	0	0	0
Total	**41**	**92**	**2**	**4**	**13**	**36**	**60**	**58**	**0**

10. Diagnostic Procedures

Table 8: Diagnostic procedures conducted at health facilities, Jan-March 2010

District	X-Ray			Ultra-Sound		
	Chest	Extremities	Others	Gyn/Obs	Abdomen	Others
Bumthang	68	66	44	0	0	0
Chukha	591	365	209	667	692	198
Dagana	0	0	0	0	0	0
Gasa	0	0	0	0	0	0
Lhuentse	71	35	22	0	16	0
Mongar	762	347	287	517	430	26
Paro	183	141	89	0	0	0
Pemagatshel	36	9	12	0	0	0
Punakha	142	153	36	474	209	6
SamdrupJongkhar	161	100	50	102	70	78
Samtse	319	203	136	0	0	0
TrashiYangtse	11	3	2	0	0	0
Tsirang	290	36	20	86	35	0
Zhemgang	64	36	33	0	0	0
Total	**2698**	**1494**	**940**	**1846**	**1452**	**308**

11. Dental Services

Table 9: Dental services availed by people at health facilities, Jan-March 2010

District Name	Extractions	Filling	Scaling	Prophylaxis	Others
Bumthang	278	140	0	9	251
Chukha	750	700	18	23	1780
Dagana	60	45	0	3	96
Gasa	0	0	0	0	0
Lhuentse	65	126	6	2	114
Mongar	350	261	8	17	583
Paro	437	671	13	23	1068
Pemagatshel	49	58	0	2	30
Punakha	168	119	3	38	229
SamdrupJongkhar	315	108	3	10	131
Samtse	159	405	0	229	260
TrashiYangtse	75	57	0	12	136
Tsirang	162	161	0	70	177
Zhemgang	76	37	2	9	205
Total	**2944**	**2888**	**53**	**447**	**5060**

12. TB Report

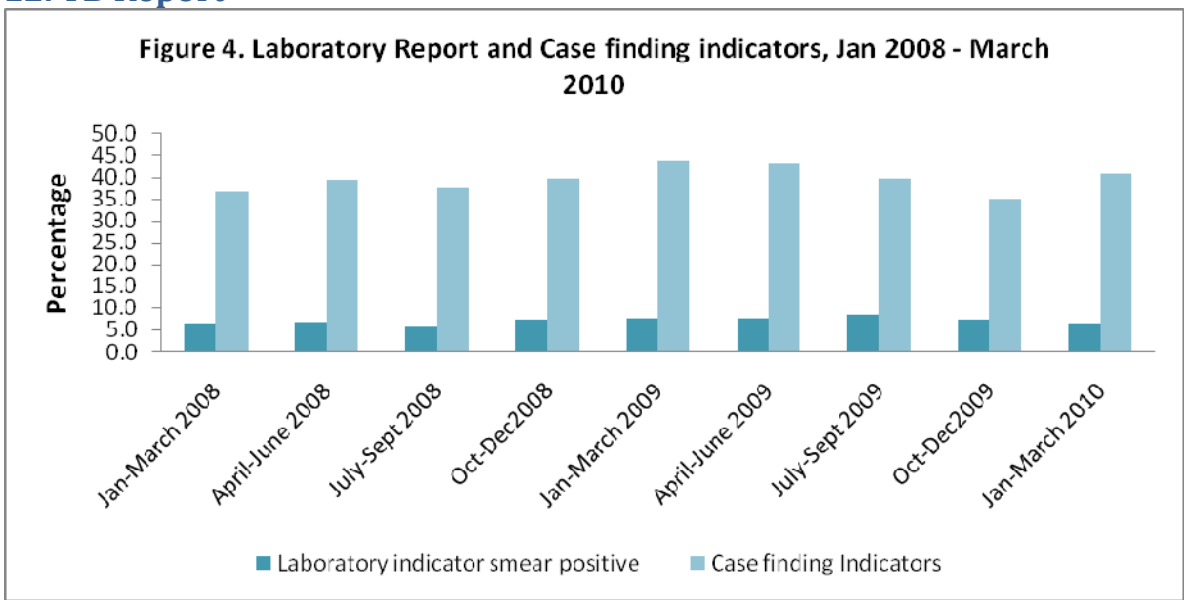
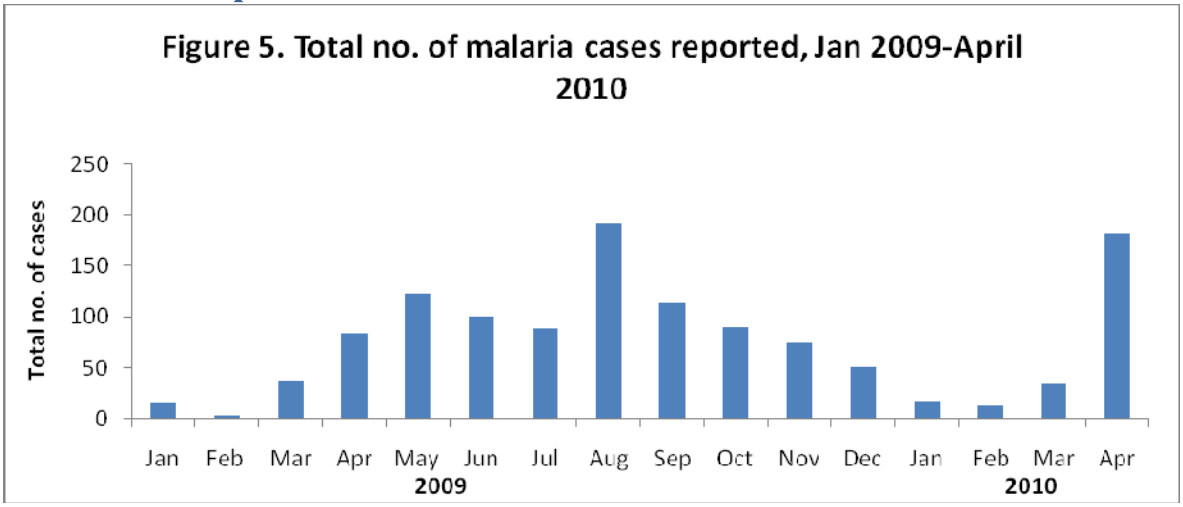


Table 10: Treatment outcome indicators, Jan-March 2009

Indicators	New P Positive	Relapse	Failure	Default
Cure rate	85.3	77.8	66.7	100
Completed rate	3.9	11.1	0	0
Success rate	89.2	88.9	66.7	100
Mortality D/A	2.9	0	0	0
Failure rate	6.9	11.1	33.3	0
Default rate	0.98	0	0	0

13. Malaria Report

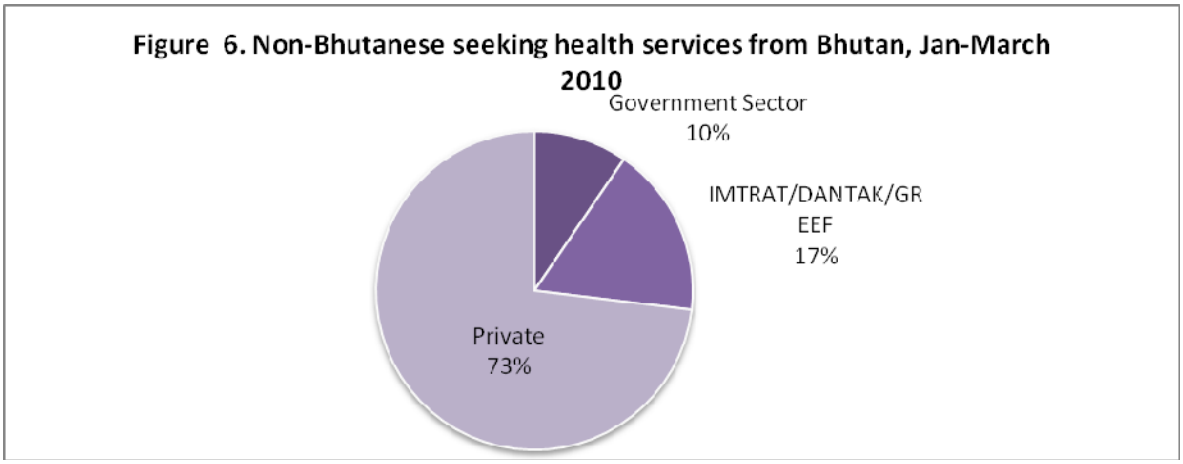


14. Non-Bhutanese seeking health services

Table 11: Health services availed by non-Bhutanese, Jan-March 2010

District_Name	Government Sector	IMTRAT/DANTAK/GREEF	Private
Bumthang	5	0	73
Chukha	50	327	230
Dagana	4	3	115
Gasa	0	0	0
Lhuentse	2	4	116
Mongar	15	0	207
Paro	7	135	239
Pemagatshel	3	0	66
Punakha	16	1	182
SamdrupJongkhar	5	234	114
Samtse	52	0	1241
TrashiYangtse	8	1	52
Tsirang	200	0	47
Zhemgang	20	0	282
Total	**387**	**705**	**2964**

*The report is only for the district hospitals



From Pg. 1

To effectively treat such cases, early diagnosis is critical and sometimes long-term peritoneal dialysis is required for meningococcemia. Profound metabolic abnormalities such as hypokalemia and hypophosphatemia may occur paradoxically in the presence of oliguria in meningococcemia.

2. Case Report

A 16-year-old student was admitted in Thinlaygang BHU-I at 4.00 p.m. from Thinlaygang Middle Secondary School on 16th April with history of high fever, chill, headache and diarrhea for one day. On examination in BHU, patient BP was recorded 60/40 mmHg, temperature 98^0F, pulse not readable, respiration 40 breath per minute, dehydration(++), pallor (+) and cyanosis(+). Patient was managed with i.v. RL and NS and Tab maxeron 1 tab stat for dehydration and vomiting to stabilize BP. After one hour of admission vitals were rechecked at 5.00 p.m., and BP was recorded 90/60 mmHg, pulse 90 beats per minutes and heart rate 104 beats per minutes. Patient was then referred to JDWNRH with parents around 5.30 p.m. During one hour of observation in BHU, patient had vomited once.

Patient reported to Casualty Department, JDWNRH at 8.20 p.m. Patient was examined by doctor on evening duty and recorded BP 100/60 mmHg, temperature 103^0F but had no dehydration. Patient was administered Tab PCM 2 tabs stat x tds, Tab Septran and i.v. RL and NS to control fever and improve BP. Patient was kept in Casualty for observation. Lab tests advised were CBC,

RFT, LFT, blood MP, widal, dengue. The CBC and RFT test results showed thrombocytopenia and renal insufficiency. MP, widal and dengue test results were negative (Table 1).

At 9.20 p.m. patient was examined by doctor on night duty and observed erythromatous patches scattered all over the body with high fever. BP was recorded 100/60 mm Hg and respiration 92 breath/minute rate. Doctor advised to administer i.v. Maxeron stat and advised lab tests BT/CT, stool RE. However, BT/CT lab test result was not available with patient history record.

At 11.30 p.m., doctor on duty re-examined the patient and found no sign of improvement. Doctor contacted physician and on verbal instruction from physician, patient was administered i.v. Ceftriaxone, i.v. Ranitidine and blood transfusion. Lab tests advised were RFT and LFT but test result was not available with record.

Table 1*: Laboratory results at admission time (8.20 p.m)*

Test parameter	Result	Unit
WBC	5.2	$x10^3$/ul
Lymphocytes	**16.0**	%
Neutrophils/Gran	**77.0**	%
Monocytes	3.0	%
Basophil	0	%
Eosinophil	0	%
RBC	4.7	$x10^6$/ul
Hemoglobin	13.2	%
Hematocrit	36.0	%
Platelet	**94.0**	$x10^3$/ul
Widal	Normal titer	
Dengue Serology (IgM)	Negative	
Urea	**56.0**	mg/dl
Creatinine	**2.4**	mg/dl
Sodium	**131.0**	mEq/l
Potassium	**3.0**	mEq/l
Chloride	98.0	mEq/l

At 12.45 a.m. patient was **managed for dengue hemorrhage fever (DHF) and myocarditis.** Patient was administered inj. dopamine, inj. hydrocortisone, inj. chromostat and platelet

transfusion. Patient BP had improved after administration of dopamine (Figure 1) but fever and erythromatous patches did not subside. Additional lab tests CBC, LDH and CK-MB were advised. Lab result showed thrombocytopenia and elevated level of CK-MB (Table 2 &3).

Figure 1: Course of blood pressure and its management

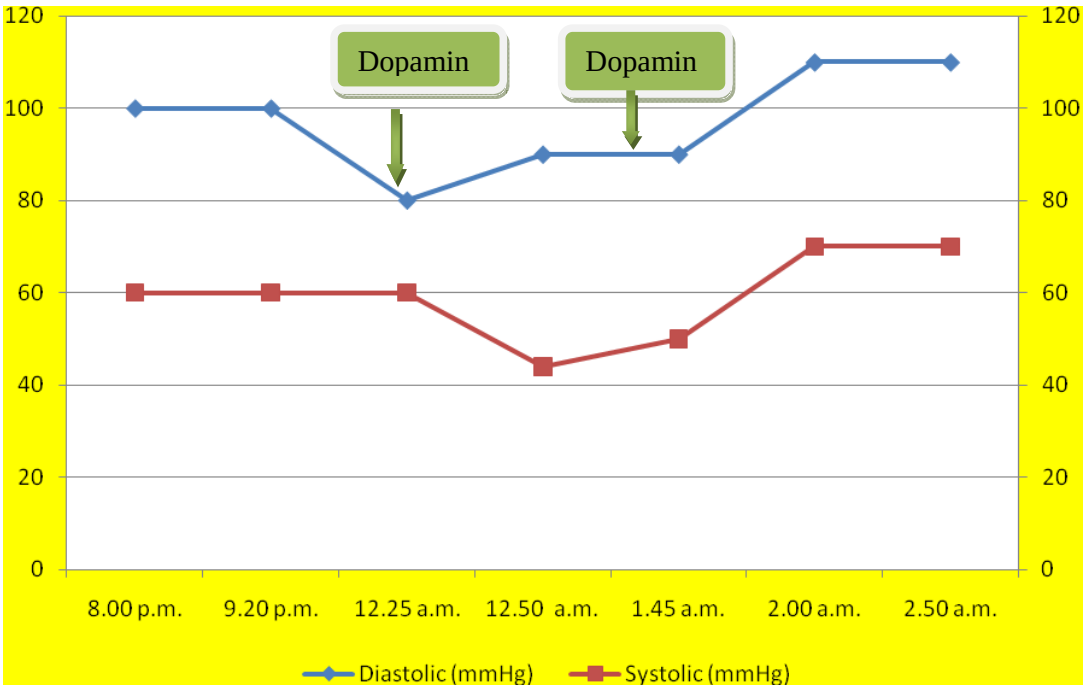


Table 2*: Laboratory results at 00.58 a.m.*

Test parameter	Result	Unit
WBC	6.1	$x10^3$/ul
Lymphocytes	18.0	%
Neutrophils/Gran	74.0	%
Monocytes	5.0	%
Basophil	0	%
Eosinophil	0	%
RBC	4.22	$x10^6$/ul
Hemoglobin	13.2	%
Hematocrit	32.0	%
Platelet	**16.0**	$x10^3$/ul

Table 3*: Laboratory result at 00.58 a.m.*

Test parameter	Result	Unit
LDH	346	IU/L
CK-MB	**122**	IU/L

At 2.00 a.m. patient was observed irritable and oxygen was administered. At 3.05 a.m. patient began gasping with frothiness + and died at 3.45 a.m. Cause of death was declared as **septicemia shock/? dengue hemorrhage fever + myocarditis + renal involvement /? meningococcal septicemia**.

3. Discussion

Neisseria meningitidis is divided into 13 serogroups based on capsular polysaccharide structure but only six sero-groups (A, B, C, W-135, X and Y) cause life-threatening diseases. Although sero-group typing was not done for this patient but reference from various article suggested serogroup A as causative agent because sero-group A cause frequent epidemic in the South Asia region and also the case was from school where meningococcal meningitis outbreak was confirmed.

As per the information available in case history of patient, the student has visited BHU with sudden onset of fever, chills and myalgia and initial management with RL and NS fluid in BHU showed clinical improvement but concealing the ongoing deterioration which is the general phenomenon of bacterial septicemia that leads to shock. In nearly all patients who develop shock by meningococci infection and in most patients with meningitis, the beginning of the bacteremic phase is marked by the onset of chillis, acute fever, low-back pain and generalized muscle aches. In invasive meningococcal disease, once viable meningococci reach the bloodstream and if bacteremia is not cleared, clinically overt disease develops. In such cases, the ultimate clinical presentation is determined by bacterial properties such as endotoxin release, host factors such as immune status and possible endotoxin responsiveness. In meningococcal infection, endotoxin-induces pro-inflammatory cytokine such as tumor necrosis factor (TNF) and anti-inflammatory interleukin-10 (IL-10) which leads to septic shock called fulminant meningococcal sepsis (FMS) or meningococcemia within a few hours without any signs of meningitis. This condition is

characterized by high concentrations of endotoxin and cytokines in plasma. Therefore, early diagnosis of FMS is extremely difficult because of confusing signs and symptoms at the early stage. Although one of the striking features of meningococci is their propensity to invade the meanings but patients with less marked bacterial proliferation in the bloodstream and less cytokinemia present meningitis only after 18 -36 hours.

FMS is characterized by shock and disseminate intravascular coagulation (DIC); two interrelated process. Shock is caused by capillary leakage, inappropriate vascular tone, intravascular microthrombi and myocardial dysfunction. The central activator that elicits these derangements is meningococcal endotoxin and the severity of shock correlates with the degree of endotoxinemia. One of the typical features of FMS is myocardial depression caused by endovascular thrombosis, vasculitis, and a circulating myocardial depressant factors (possibly tumor necrosis factors (TNF) or interleukin factor -1 (IL-1)) that reaches its maximum within few hours after admission. The myocardial dysfunction was found associated in this patient with high level of CK-MB enzyme in blood test (Table 3). Echocardiography performed at this time would have shown an increased end-diastolic volume and decreased left ventricular shortening fraction.

DIC manifestation; skin hemorrhages is the hallmark of invasive meningococcal disease. Skin hemorrhages were found developed in this patient (16 years old boy) all over the body within 6 hours of onset of disease, but the diagnosis was missed because the initial skin manifestations resembled a viral rash. However, CBC showed elevated neutrophil count consistently (Table 1 &2) clearly suggesting bacterial infection. Microscopically, skin lesions/hemorrages are characterized by endothelial damage and hemorrhages around and microthrombi in small vessels, consistent with generalized Sanarelli-Shwartzman reaction. The lesions are reflection of the endotoxin and cytokine-primed vasculitis that is mediated by the up-regulation of adhesion molecules on endothelium and degranulating activated neutrophilis. Clinically, they are visual manifestation of DIC and consumption coagulopathy.

Although DIC is a generalized phenomenon affecting all organs, the adrenals are particularly vulnerable. In this patient (16 yrs old), the involvement of renal was evident from RFT result that showed elevated of urea, creatinine and electrolytes; the test done during admission (Table 1). The subsequent RFT would have helped to substantiate the finding but no result was available although RFT test was advised. Adrenal hemorrhages usually lead to transitory adrenal insufficiency and then to acute renal failure in FMS.

In meningococcal infections, severe DIC is associated with a very poor prognosis and study has shown that an increased activity of tissue factors (TF); a cell mediator on monocytes is associated with high mortality rate. The mortality rate of FMS varies from 20-80% in different studies conducted. Clinical deterioration is overwhelming, and approximately half of the patients who die will do so within 24 hours after the first symptoms occur. Studies have shown that one-third of patients with fatal disease die within 6 hours after hospital admission and one-third die between 6 and 18 hours. Any recovered patients may be complicated by hemorrhages, ARDS, anuria, and multiple organ failure. Skin and limb necrosis would require amputation or plastic surgery in 10-20% of FMS recovered patients.

In acute meningococcal disease in particular FMS, early diagnosis and recognition of patient at risk are crucial for the timely start of life saving antibiotic and anti-shock therapy. If antibiotic therapy is started later in the course of the disease, i.e. when ischemia lesions have progressed, more bacteria can easily escape the effect of antibiotic because meningococci remain viable in the nonperfused centre of these lesions for up to 13 hours after the start of antibiotic therapy. That's why FMS has poor prognosis once ischemia lesions have progressed even if patient is put on antibiotic therapy as seen with this death case of 16 years-old boy. Therefore, meningococcal infection should be considered as a differential diagnosis of fever, especially in the presence of skin rash or petechiea even when there are no signs of meningitis because in FMS patients, skin rash/lesions appears within 6-12 h after the onset of disease and will die if diagnosis is missed.

4. Conclusion

The findings from case history study of death patient; a 16 years old boy from Thinlaygang Middle Secondary School clearly confirms the cause of death as fulminant meningococcal sepsis (FMS) with acute renal failure.

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The Policy and Planning Division would like to solicit reviews and feedbacks for the betterment of the publication. Suggestions, views and constructive criticism are always welcome.

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